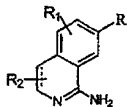




## INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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| <b>(21) International Application Number:</b> PCT/GB98/02600<br><br><b>(22) International Filing Date:</b> 28 August 1998 (28.08.98)<br><br><b>(30) Priority Data:</b><br>9718392.5                      29 August 1997 (29.08.97)                      GB<br>9803173.5                      13 February 1998 (13.02.98)                      GB<br><br><b>(71) Applicant (for all designated States except US):</b> PROTEUS MOLECULAR DESIGN LTD. [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB).<br><br><b>(72) Inventors; and</b><br><b>(75) Inventors/Applicants (for US only):</b> LIEBESCHUETZ, John, Walter [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). WYLIE, William, Alexander [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). WASZKOWYCZ, Bohdan [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). MURRAY, Christopher, William [GB/GB]; Beechfield House, Lyme Green Business Park,   |           | Macclesfield, Cheshire SK11 0JL (GB). RIMMER, Andrew, David [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). WELSH, Pauline, Mary [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). JONES, Stuart, Donald [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). ROSCOE, Jonathan, Michael, Ernest [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). YOUNG, Stephen, Clinton [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). MORGAN, Phillip, John [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). CAMP, Nicholas, Paul [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB). CREW, Andrew, Phillip, Austin [GB/GB]; Beechfield House, Lyme Green Business Park, Macclesfield, Cheshire SK11 0JL (GB).<br><br><b>(74) Agents:</b> COCKBAIN, Julian et al.; Frank B. Dehn & Co., 179 Queen Victoria Street, London EC4V 4EL (GB).<br><br><b>(81) Designated States:</b> AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).<br><br><b>Published</b><br><i>With international search report.</i> |
| <b>(54) Title:</b> 1-AMINO-7-ISOQUINOLINE DERIVATIVES AS SERINE PROTEASE INHIBITORS<br><br><div style="text-align: center;">  </div><br><b>(57) Abstract</b><br><br>The invention relates to serine protease inhibitor compounds of formula (I) where R <sub>1</sub> is hydrogen, halo, cyano, nitro or hydroxyl, amino, alkoxy, alkyl, aminoalkyl, hydroxyalkyl, thiol, alkylthio, aminosulphonyl, alkoxyalkyl, alkoxyacarbonyl, acyloxymethoxycarbonyl or alkylamino optionally substituted by hydroxy, alkylamino, alkoxy, oxo, aryl, cycloalkyl, amino, halo, cyano, nitro, thiol, alkylthio, alkylsulphonyl, alkylsulphenyl, alkylsulphonamido, alkylaminosulphonyl, haloalkoxy and haloalkyl; R <sub>2</sub> is hydrogen, halo, methyl, amino, hydroxy, or oxo; and R is X-X-Y(R <sub>7</sub> )-L-Lp(D) <sub>n</sub> ; wherein each X independently is a C, N, O or S atom or a CO, CR <sub>1</sub> , C(R <sub>1</sub> ) <sub>2</sub> or NR <sub>1</sub> group, at least one X being C, CO, CR <sub>1</sub> or a C(R <sub>1</sub> ) <sub>2</sub> group; Y (the α-atom) is a nitrogen atom or a CR <sub>1</sub> group or Y and L taken together form a cyclic group; R <sub>7</sub> is a lipophilic group selected from alkyl, alkenyl, mono- or bi-cycloalkyl, aryl, heteroaryl, mono- or bicycloalkylalkyl, mono- or bicycloalkylalkenyl, aralkyl, heteroaryl-alkyl, arylalkenyl, heteroarylalkenyl all optionally substituted by a group R <sub>1</sub> ; L is an organic linker group containing 1 to 5 backbone atoms selected from C, N, O and S, or a branched alkyl or cyclic group; Lp is a lipophilic organic group selected from alkyl, heterocyclic, alkenyl, alkaryl, cycloalkyl, polycycloalkyl, cycloalkenyl, aryl, aralkyl or haloalkyl group or a combination of two or more such groups optionally substituted by one or more of oxa, thia, aza or R <sub>1</sub> groups; D is a hydrogen bond donor group; and n is 0, 1 or 2 and salts thereof. |           |  |